Antenatal Diagnosis of Genetic Disease

Genetic disorders such as chromosome abnormalities or biochemical defects may be diagnosed antenatally by amniocentesis and examination of the amniotic fluid or cells. Amniotic fluid is obtained by trans-abdominal aspiration in early pregnancy without significant hazard to mother or infant. The fluid and amniotic (fetal) cells are then examined directly, or the amniotic cells are cultured for subsequent biochemical or cytological tests.

Amniocentesis for detection of chromosome disorders may be indicated in older mothers who have an increased risk of giving birth to infants with Down's syndrome (mongolism), and in pregnancy where a parent is known to be a carrier of a translocation or other chromosome abnormality. The mother who is anxious about her pregnancy because of a previous child with Down's syndrome may also request amniocentesis for chromosome analysis of fetal cells.

In families known to be affected with sex-linked disorders, such as classical hemophilia or Duchenne muscular dystrophy, the determination of fetal sex by examination of chromatin (Barr) bodies and chromosome analysis of the cultured fetal cells gives additional information regarding the probability that the present fetus is affected.

The number of biochemical disorders that can be diagnosed in utero is small at present, but rapidly increasing. Prenatal diagnosis by biochemical tests on the amniotic fluid and cells has been made in the instance of the mucopolysaccharidoses, Lesch-Nyhan syndrome, galactosemia, glycogen storage disease type II (Pompe's disease), and Tay Sachs disease.

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Septic Abortion: Current Management

The management of septic abortion continues to improve. Trends of importance are: (1) earlier and improved diagnosis; and (2) prompt and aggressive treatment. Initial treatment must be based upon a clinical diagnosis. A delay in treatment while awaiting laboratory confirmation could permit irreversible toxic processes to become established. Metabolic disorganization resulting from the circulating bacterial toxins can lead to the rapid onset of septic shock and renal failure.

Early evacuation of the uterus, along with the rapid administration of pharmacologic doses of proven antibiotics (chloramphenicol, penicillin) and steroids (Solu-Cortef,®, Solu-Medrol®), will give the patient the greatest possible advantage. Total abdominal hysterectomy with bilateral salpingo-oophorectomy in cases of early treatment failure, or in cases of welchii infection, has contributed significantly to the saving of lives.

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RhoGam®—Current Status

The obstetrician is in the key position to implement the ultimate elimination of hemolytic disease of the newborn due to Rh incompatibility, as a cause of perinatal mortality and morbidity. The universal availability of high titer anti-Rh_o(D) immune globulin (RhoGam®), plus the legislative requirement recently enacted in California requiring Rh testing and reporting on all pregnant women, should ensure that all unsensitized Rh-negative women will be given RhoGam following known termination of any pregnancy beyond 12 weeks' (first trimester) duration. There is increasing evidence, based on therapeutic abortion studies, that termination of pregnancy even in the early months permits entry of fetal cells into the maternal circulation, particularly when the termination includes intra-

uterine manipulation. We have documented profound maternal sensitization following incomplete spontaneous abortion at 12 weeks followed by dilatation and curettage.

RhoGam should be given in indicated cases within 72 hours of delivery or termination of pregnancy, after proper cross-matching with the mother's blood. If the patient refuses RhoGam for any reason, suitable medicolegal documentation of such refusal should be carried in the patient's record. RhoGam should be repeated following each Rh positive or Rh unknown pregnancy, provided the Rh negative mother has not been previously sensitized by pregnancy or blood administration.

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Squamous Dysplasia of the Uterine Cervix

There is evidence that squamous neoplasia of the uterine cervix progresses from squamous dysplasia to carcinoma in situ, microinvasive carcinoma, and infiltrative carcinoma.

The evidence for progression is by: (1) clinical observation in one-third of cases, dysplasia when untreated progresses to intraepithelial carcinoma over a five-year period; (2) DNA content of the nuclei of the involved epithelium (the percent of aneuploid cells rises progressively through the four stages); and (3) growth characteristics in tissue culture (the observed repelling characteristic of cells in monolayer cultures increases from dysplasia through infiltrative carcinoma).

Cervical dysplasias present special problems for clinicians. Generally there is no gross lesion visible; most often, a Class III cervical cytology report is the first sign of its presence. Occasionally the colposcopist or colpomicroscopist will observe the epithelial change. Most often the clinician will take a biopsy specimen from the squamocolumnar junction and proceed to cervical conization to define the extent of the change and to rule out invasive cancer.

Cytologists and colposcopists are able accurately to predict about 60 percent of dysplasias as later identified by histologic verification. Eventually the diagnosis must be made by histologic sections. The most complete histologic appraisal is the full cervical conization and this diagnostic procedure generally rules out invasive cancer, and serves for treatment.

If invasive or intraepithelial cancer could be excluded with relative certainty by procedure less extensive than surgical conization, a substantial amount of morbidity could be avoided. To this end, the colposcope, the endocervical curettage, and the four quadrant directed biopsies have been utilized. Reliance on this outpatient diagnostic appraisal requires identification of a transformation zone, a cervical canal capable of allowing endocervical curettage (ECC), and a willingness to proceed to conization if these fail.

Treatment rests on these assumptions: (1) if neoplasia is present, it will be present in the squamocolumnar junction; and (2) if the squamocolumnar junction and abnormal areas of the exocervix show only dysplasia and if the endocervical curettage is negative, intraepithelial or infiltrative carcinoma are excluded. It is generally true in postmenopausal women that the transformation zone is not visualized by colposcopy and the cervical canal is difficult to currette. Consequently a postmenopausal woman is not definitively evaluated in an outpatient department.

Once squamous dysplasia has been established and more advanced neoplasia excluded, under controlled conditions treatment may rest at: (1) electrocautery; (2) cryosurgery; (3) cervical conization (preferred). Hysterectomy is generally not indicated for squamous dysplasia alone.

In view of the malignant potential of squamous dysplasia, all patients require periodic follow-up with cytologic screening following treatment.

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